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Search Results -

Term	Documents
1BETA	1019
1BETAS	0
(1BETA AND 12).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	10
(L12 AND 1BETA).USPT,PGPB,JPAB,EPAB,DWPI,TDBD.	10

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L14

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DATE: Sunday, December 14, 2003 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L14	L12 and 1beta	10	L14
L13	L12 and beta1	1	L13
L12	L11 and beta	78	L12
L11	l3 and cancer	138	L11
L10	l3 cancer	7	L10
L9	wang-li-ming.in.	15	L9
L8	shelness-grgory.in.	0	L8
L7	childers-steven.in.	1	L7
L6	mach-robert-h.in.	3	L6
L5	wheeler-kenneth-t.in.	2	L5
L4	sigma-1beta	0	L4
L3	sigma$5 receptor	650	L3
L2	sigma1beta	1	L2
L1	sigma1beta receptor	1	L1

END OF SEARCH HISTORY

STIC-Biotech/ChemLib 10/085586

From: Basi, Nirmal
Sent: Tuesday, November 18, 2003 2:57 PM
To: STIC-Biotech/ChemLib
Subject: sequence search for 09/823,069

App. #: 09/832,069
Result format: Paper.
Title:Methods and composition utilizing an alternative splice variant of sigma-1 receptor
Inventors:Wheeeler at al
Priority Date:4/3/200

Please search:
i) SEQ ID NO:1, 2

Search commercial and issued database.

Thanks,
Nirmal S. Basi

Searcher:_____
Phone:_____
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Date Picked Up:_____
Date Completed:_____
Searcher Prep/Review:_____
Clerical:_____
Online time:_____

TYPE OF SEARCH:
NA Sequences:_____
AA Sequences:_____
Structures:_____
Bibliographic:_____
Litigation:_____
Full text:_____
Patent Family:_____
Other:_____

VENDOR/COST (where applic.)
STN:_____
DIALOG:_____
Questel/Orbit:_____
DRLink:_____
Lexis/Nexis:_____
Sequence Sys.:_____
WWW/Internet:_____
Other (specify):_____

FILE 'MEDLINE'
FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> s sigma1beta receptor#
L1 1 SIGMA1BETA RECEPTOR#

=> s sigma1 receptor#
L2 384 SIGMA1 RECEPTOR#

=> s l2 and beta
L3 21 L2 AND BETA

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 14 DUP REM L3 (7 DUPLICATES REMOVED)

=> d l1

L1 ANSWER 1 OF 1 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-662943 [76] WPIDS
DNC C2001-194735
TI Novel isolated polynucleotide encoding ***sigma1beta*** ***receptor*** useful in screening assay to identify ligands specific for the ***sigma1beta*** ***receptor*** for tumor imaging, diagnostic and treatment methods.
DC B04 D16
IN CHILDERS, S; MACH, R H; SHELNESS, G; WANG, L; WHEELER, K T
PA (UYWA-N) UNIV WAKE FOREST; (CHIL-I) CHILDERS S; (MACH-I) MACH R H; (SHEL-I) SHELNESS G; (WANG-I) WANG L; (WHEE-I) WHEELER K T
CYC 95
PI WO 2001074297 A2 20011011 (200176)* EN 56p A61K000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001087287 A 20011015 (200209) A61K000-00
US 2002061847 A1 20020523 (200239) A61K038-17
ADT WO 2001074297 A2 WO 2001-US10650 20010330; AU 2001087287 A AU 2001-87287 20010330; US 2002061847 A1 Provisional US 2000-193694P 20000331, US 2001-823069 20010330
FDT AU 2001087287 A Based on WO 2001074297
PRAI US 2000-193694P 20000331; US 2001-823069 20010330
IC ICM A61K000-00; A61K038-17
ICS C07H021-04; C07K014-705; C12N005-06; C12P021-02

=> d ibib abs l3 1-21

L3 ANSWER 1 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2000028702 MEDLINE
DOCUMENT NUMBER: 20028702 PubMed ID: 10562962
TITLE: Anti-amnesic effects of sigma (sigma)-receptor agonists.
AUTHOR: Matsuno K
CORPORATE SOURCE: Discovery Research Division, Santen Pharmaceutical Co., Ltd., Osaka, Japan.
SOURCE: NIPPON YAKURIGAKU ZASSHI. FOLIA PHARMACOLOGICA JAPONICA, (1999 Jul) 114 (1) 25-33. Ref: 50
Journal code: 0420550. ISSN: 0015-5691.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000121
AB Both traditional and novel sigma (sigma)-receptor agonists have been reported to possess anti-amnesic effects in rodents. In particular, the anti-amnesic effects induced by the novel ***sigma1*** - ***receptor*** agonists, such as (+)-pentazocine, SA4503 and PRE-084, were shown in ***beta*** amyloid-peptide-induced, basal forebrain (BF)-lesioned and carbon monoxide (CO)-induced amnesia models and senescence-accelerated mouse (SAM). In addition, these ***sigma1*** - ***receptor*** agonists have good profiles for the central acetylcholine and dopamine systems. Moreover, they also have neuroprotective and anti-depressive effects. These evidence suggested that the ***sigma1*** - ***receptor*** agonists may be promising compounds for the treatment of dementing disorders such as Alzheimer's disease, senile dementia and vascular dementia. However, the sigma-receptor family is still considered to be enigmatic molecular targets. More molecular cloning and biochemical studies on the sigma-receptor family are needed.

L3 ANSWER 2 OF 21 MEDLINE on STN
ACCESSION NUMBER: 1999330295 MEDLINE
DOCUMENT NUMBER: 99330295 PubMed ID: 10403501
TITLE: Ligands for opioid and sigma-receptors improve cardiac electrical stability in rat models of post-infarction cardiosclerosis and stress.
AUTHOR: Lishmanov YuB; Maslov L N; Naryzhnaya N V; Tam S W
CORPORATE SOURCE: Department of Experimental Cardiology, Institute of Cardiology, Tomsk, Russia.
SOURCE: LIFE SCIENCES, (1999) 65 (1) PL13-7.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990723
AB The effects of the extremely selective mu-opioid receptor agonist, [D-Arg2,Lys4]-dermorphin-(1-4)-amide (DALDA), the mu-opioid receptor agonist morphine, the mu/delta agonist D-Ala2, Leu5, Arg6-enkephalin (dalargin), the kappa-opioid receptor agonist spiradoline, and the ***sigma1*** - ***receptor*** antagonist DuP 734 on ventricular fibrillation threshold (VFT) was investigated in an experimental post-infarction cardiosclerosis model and an immobilization stress-induced model in rats. Both models produced a significant decrease in VFT. The postinfarction cardiosclerosis-induced decrease in VFT was significantly reversed by intravenous administration of dalargin (0.1 mg/kg), DALDA (0.1 mg/kg), or morphine HCl (1.5 mg/kg). Pretreatment with naloxone (0.2 mg/kg) completely eliminated the increase in cardiac electrical stability produced by DALDA. Both spiradoline (8 mg/kg, i.p.) and DuP 734 (1 mg/kg, i.p.) produced a significant increase in VFT in rats with post-infarction cardiosclerosis. This effect of spiradoline was blocked by nor-binaltorphimine. The immobilization stress-induced decrease in VFT was significantly reversed by administration of either DALDA, spiradoline or DuP 734. In conclusion, activation of either mu- or kappa1-opioid receptors or blockade of ***sigma1*** - ***receptors*** reversed the decrease in VFT in both cardiac compromised models. Since DALDA and dalargin essentially do not cross blood brain barriers, their effects on VFT may be mediated through peripheral mu-opioid receptors.

L3 ANSWER 3 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:424096 BIOSIS
DOCUMENT NUMBER: PREV200300424096
TITLE: Cloning of an emopamil-binding protein (EBP)-like protein that lacks sterol DELTA8-DELTA7 isomerase activity.
AUTHOR(S): Moebius, Fabian F. [Reprint Author]; Fitzky, Barbara U.; Wietzorrek, Georg; Haidekker, Alexander; Eder, Andrea; Glossmann, Hartmut
CORPORATE SOURCE: Institut fuer Biochemische Pharmakologie, Peter-Mayr-Strasse 1, A-6020, Innsbruck, Austria Fabian.Moebius@uibk.ac.at
SOURCE: Biochemical Journal, (15 August, 2003) Vol. 374, No. 1, pp. 229-237. print.
ISSN: 0264-6021.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: DDBJ-AF034544; EMBL-AF034544; GenBank-AF034544; DDBJ-AF243433; EMBL-AF243433; GenBank-AF243433; DDBJ-U795328; EMBL-U795328; GenBank-U795328; DDBJ-Z37986; EMBL-Z37986; GenBank-Z37986
ENTRY DATE: Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003
AB EBP (emopamil-binding protein) is a high-affinity binding protein for (3H)emopamil and belongs to the family of so-called sigma receptors. Mutations that disrupt EBP's 3beta-hydroxysteroid sterol DELTA8-DELTA7 isomerase activity (EC 5.3.3.5) impair cholesterol biosynthesis and cause X-chromosomal dominant chondrodysplasia punctata. We identified a human cDNA for a novel EBPL (EBP-like protein) with a calculated mass of 23.2 kDa. Amino acid sequence alignments and phylogenetic analysis revealed that EBPL is distantly related to EBP (31% identity and 52% similarity) and found in animals but not in plants. EBPL is encoded by four exons on human chromosome 13q14.2 covering 30.7 kb, and a partially processed EBPL pseudogene was found on 16q21. The EBPL mRNA was expressed ubiquitously and most abundant in liver, lung and kidney. Upon heterologous expression in yeast EBPL had no detectable 3beta-hydroxysteroid sterol DELTA8-DELTA7 isomerase and sigma-ligand-binding activity. Nine out of ten amino aci residues essential for catalytic activity of EBP were conserved in EBPL. Replacement of the only differing residue (EBP-Y111W) reduced catalytic activity of EBP. Transfer of the divergent residue from EBP to EBPL (EBPL-W91Y) and chimaerization of EBP and EBPL at various positions failed to restore catalytic activity of EBPL. Chemical cross-linking induced homodimerization of EBPL and EBP. Whereas mevinolin increased the mRNA for EBP and DHCR7 (DELTA7-sterol reductase) in HepG2 cells, it had no effect on mRNAs for EBPL and ***sigma1*** ***receptor*** , indicating that EBP and EBPL expression are not coordinated. We propose that EBPL has a yet-to-be-discovered function other than cholesterol biosynthesis.

L3 ANSWER 4 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:223620 BIOSIS
DOCUMENT NUMBER: PREV200300223620
TITLE: Anti-amnesic effect of dimemorfan in mice.
AUTHOR(S): Wang, Hui-Hung; Chien, Jyh-Wei; Chou, Yueh-Ching; Liao, Jyh-Fei [Reprint Author]; Chen, Chieh-Fu
CORPORATE SOURCE: Department and Institute of Pharmacology, National Yang-Ming University, No. 155, Sec. 2, Li-Nong Street, Taipei, 112, Taiwan jfliao@ym.edu.tw
SOURCE: British Journal of Pharmacology, (March 2003) Vol. 138, No. 5, pp. 941-949. print.
ISSN: 0007-1188 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 May 2003
Last Updated on STN: 7 May 2003
AB 1. Dimemorfan, an antitussive for more than 25 years, has previously been reported to be a relative high-affinity ligand at sigma-1 (***sigma1***) ***receptor*** with the Ki value of 151 nM. 2. To test whether dimemorfan has anti-amnesic effects similar to a ***sigma1*** ***receptor*** agonist, this study examined its effects on scopolamine- and ***beta*** -amyloid peptide-(25-35)-induced amnesia in mice. 3 Dimemorfan (10-40 mg kg-1, i.p.) administered 30 min before the training trial, immediately after the training trial, or 30 min before the retention test significantly improved scopolamine (1 mg kg-1, i.p.)- or ***beta*** -amyloid peptide-(25-35) (3 nmol mouse-1, i.c.v.)-induced amnesia in a step-through passive avoidance test. Dimemorfan (5-40 mg kg-1, i.p.) pretreatment also attenuated scopolamine (8 mg kg-1, i.p.)-induced amnesia in a water-maze test. And, these anti-amnesic effects of dimemorfan, like the putative ***sigma1*** ***receptor*** agonist (+)-N-allylnormetazocine ((+)-SKF-10047), were antagonized by a sigma receptor antagonist haloperidol (0.25 mg kg-1, i.p.). 4. These results indicated that dimemorfan has anti-amnesic effects and acts like a ***sigma1*** ***receptor*** agonist.

L3 ANSWER 5 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:551466 BIOSIS
DOCUMENT NUMBER: PREV200200551466
TITLE: Enhanced antidepressant effect of sigma1 (***sigma1***) ***receptor*** agonists in beta25-35-amyloid peptide-treated mice.
AUTHOR(S): Urani, Alexandre; Romieu, Pascal; Roman, Francois J.; Maurice, Tangui [Reprint author]
CORPORATE SOURCE: CNRS UMR 5102, University of Montpellier II, Place Eugene Bataillon, 34095, C.C. 090, Montpellier Cedex 5, France maurice@univ-montp2.fr
SOURCE: Behavioural Brain Research, (21st August, 2002) Vol. 134, No. 1-2, pp. 239-247. print.
CODEN: BBREDI. ISSN: 0166-4328.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002
AB This study examined the antidepressant efficacy of the selective ***sigma1*** ***receptor*** agonists igmesine or PRE-084 in mice injected intracerebroventricularly (i.c.v.) with beta25-35-amyloid peptide and submitted to the forced swim test. beta25-35 peptide-injected animals developed memory deficits after 8 days contrarily to controls injected with scrambled beta25-35 peptide or vehicle solution. In the forced swim test, the i.c.v. treatment failed to affect the immobility duration, but the antidepressant effect of the sigma1 agonists was facilitated in beta25-35 animals. Igmesine reduced immobility duration at 30 versus 60 mg/kg in control groups. PRE-084 decreased immobility duration at 30 and 60 mg/kg only in beta25-35 animals. Desipramine reduced the

immobility
duration similarly among groups and fluoxetine appeared less potent in beta25-35 animals. The beta25-35 animals exhibited decreased progesterone
levels in the hippocampus (-47%). The behavioural efficacy of sigma1 agonists is known to depend on neuro(active)steroids levels synthesised by
glial cells and neurones, which are affected by the ***beta*** -amyloid
toxicity. This behavioural study suggests that sigma1 agonists, due to their enhanced efficacy, may allow to alleviate the depressive symptoms associated with Alzheimer's disease.

L3 ANSWER 6 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:575419 BIOSIS
DOCUMENT NUMBER: PREV200100575419
TITLE: Enhanced antidepressant effect of sigma1 (sigma1) agonists
in ***beta*** -amyloid peptide-treated rodents.
AUTHOR(S): Urani, A. [Reprint author]; Romieu, P.; Roman, F. J. [Reprint author]; Noda, Y.; Kamei, H.; Tran, M. H.; Nagai, T.; Nabeshima, T.; Maurice, T.
CORPORATE SOURCE: Biochimie/Enzymologie, Pfizer GRD, Fresnes, France
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1,
pp. 853. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2001
Last Updated on STN: 25 Feb 2002
AB The ***sigma1*** ***receptor*** is a 223 amino acide protein involved in numerous behavioral effects. In particular, ***sigma1*** ***receptor*** agonists present potent antidepressant-like effects in several animal models of behavioral despair. The antidepressant efficacy
of selective sigma1 agonists was studied in two models of ***beta*** -amyloid-induced cognitive deficits. First, in mice injected centrally with beta25-35-amyloid peptide and submitted ten days after to forced swim
test. In this test, igmesine appeared more efficient in beta25-35 animals, by reducing immobility at 30 mg/kg vs. 60 mg/kg in control groups. Such facilitation was not observed with desipramine. Furthermore, beta25-35 animals exhibited decreased progesterone levels in
the hippocampus (-47%). Second, in rats infused during 14 days with the
beta1-40 amyloid peptide and submitted to the conditioned fear stress. In
this test, (+)-SKF-10,047 reduced the stress-induced motor suppression at
3 mg/kg in beta1-40 peptide infused rats, vs. 6 mg/kg in beta40-1 treated
rats. Igmesine presented an effect at 10 mg/kg in beta1-40 infused rats vs. 30 mg/kg in control rats. Neurosteroid measurements and immunohistochemical studies will also be presented. The sigma1 agonist
efficacy is known to depend on neuro(active)steroids levels, synthesized mainly by glial cells. These cells may be affected by b-amyloid toxicity. We suggest that sigma1 agonists, due to their enhanced efficacy, may improve Alzheimer's disease-related cognitive deficits.

L3 ANSWER 7 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:503651 BIOSIS
DOCUMENT NUMBER: PREV200100503651
TITLE: (11C)Raclopride binding was reduced in vivo by ***sigma1*** ***receptor*** ligand SA4503 in the mouse brain, while (11C)SA4503 binding was not by raclopride.
AUTHOR(S): Ishiwata, Kiichi [Reprint author]; Kobayashi, Tadayuki;
Kawamura, Kazunori; Matsuno, Kiyoshi; Senda, Michio
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of
Gerontology, Tokyo, Japan
ishiwata@pet.tmig.or.jp
SOURCE: Nuclear Medicine and Biology, (October, 2001) Vol. 28, No.
7, pp. 787-792. print.
ISSN: 0969-8051.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 2001
Last Updated on STN: 23 Feb 2002
AB (11C)Raclopride is widely used as a representative dopamine D2-like receptor ligand in positron emission tomography (PET) studies, and (11C)1-(3,4-dimethoxyphenethyl)-4-(3-phenylpropyl)piperazine dihydrochloride ((11C)SA4503) is a recently developed selective ligand for
mapping ***sigma1*** ***receptors*** in the brain. The striatal uptake of (11C)raclopride in mice was reduced by co-injection of an excess
amount of SA4503, in spite of the fact that raclopride had no effect on the brain uptake of (11C)SA4503 as shown in a previous study. The blocking effect of SA4503 on the striatal uptake of (11C)raclopride was dose-dependent, but disappeared by 1 h or 6 h after intraperitoneal injection of SA4503. The brain uptake of (11C)SA4503 was not affected by
a dopamine transporter inhibitor GBR 12909, nor was (11C) ***beta***
-CIT-FP inhibited by SA4503. The IC50 values of raclopride for sigma1 and
sigma2 receptor subtypes measured in vitro were 11800 nM and 4950 nM,
respectively, suggesting that the affinity was too low for (11C)raclopride
to bind in vivo to sigma receptors. On the other hand, the IC50 value of
SA4503 for dopamine D2 receptors was 470 nM, that is approximate 1/25 of
the affinity of raclopride for the dopamine D2 receptors. Therefore, possible explanations for the partial blocking effects of SA4503 on the striatal uptake of (11C)raclopride are: (1) an excess amount of SA4503 may
reduce the (11C)raclopride uptake due to its low affinity for dopamine D2
receptors, or (2) SA4503 may enhance endogenous dopamine release, which
results in the competitive inhibition of the (11C)raclopride uptake. These findings support that both (11C)raclopride and (11C)SA4503 are selective in vivo ligands for dopamine D2-like receptors and ***sigma1*** ***receptors*** , respectively, in spite of the partial
blocking effect of SA4503 on the striatal uptake of (11C)raclopride.

L3 ANSWER 8 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:477414 BIOSIS
DOCUMENT NUMBER: PREV199900477414
TITLE: Anti-amnesic effects of sigma (sigma) -receptor agonists.
AUTHOR(S): Matsuno, Kiyoshi [Reprint author]
CORPORATE SOURCE: Discovery Research Division, Santen Pharmaceutical Co.,
Ltd., Shimoshinjo, Higashiyodogawa, Osaka, 533-8651, Japan
SOURCE: Folia Pharmacologica Japonica, (July, 1999) Vol. 114, No.
1, pp. 25-33. print.
CODEN: NYKZAU. ISSN: 0015-5691.
DOCUMENT TYPE: Article
LANGUAGE: Japanese
ENTRY DATE: Entered STN: 9 Nov 1999
Last Updated on STN: 9 Nov 1999
AB Both traditional and novel sigma (sigma) -receptor agonists have been reported to possess anti-amnesic effects in rodents. In particular, the anti-amnesic effects induced by the novel ***sigma1*** - ***receptor*** agonists, such as (+) -pentazocine, SA4503 and PRE-084,
were shown in ***beta*** amyloid-peptide-induced, basal forebrain (BF)
- lesioned and carbon monoxide (CO) -induced amnesi models and senescence-accelerated mouse (SAM). In a dition, these ***sigma1*** -
receptor agonists have good profiles for the central acetylcholine
and dopamine systems. Moreover, they also have neuroprotective and anti-depressive effects. These evidence suggested that the ***sigma1***
- ***receptor*** agonists may be promising compounds for the treatment
of dementing disorders such as Alzheimer's disease, senile dementia and vascular dementia. However, the sigma-receptor family is still considered
to be enigmatic molecular targets. More molecular cloning and biochemical
studies on the sigma-receptor family are needed.

L3 ANSWER 9 OF 21 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:98297 BIOSIS
DOCUMENT NUMBER: PREV199800098297
TITLE: Sigma1 (***sigma1***) ***receptor*** agonists and
neurosteroids attenuate B22-35-amyloid peptide-induced amnesia in mice through a common mechanism.
AUTHOR(S): Maurice, T. [Reprint author]; Su, T.-P.; Privat, A.
CORPORATE SOURCE: I.N.S.E.R.M. Unite 336, Dev. Plasticite, Vieillissement du
Systeme Nerveux, 8 rue de l'Ecole Normale, 34296 Montpellier Cedex 5, France
SOURCE: Neuroscience, (March, 1998) Vol. 83, No. 2, pp. 413-428.
print.
CODEN: NRSCDN. ISSN: 0306-4522.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Feb 1998
Last Updated on STN: 6 Apr 1998
AB The sigma1 (***sigma1***) ***receptor*** agonists exert potent
anti-amnesic effects, as they apparently block the learning impairments either induced by the muscarinic receptor antagonist scopolamine, the N-methyl-D-aspartate receptor antagonist dizocilpine or inherently due to
the age-related deficits in senescence-accelerated mice. We recently described the amnesia induced by the ***beta*** -amyloid-related peptide beta25-35, administered centrally in an aggregated form, in mice.
The deficits were sensitive to cholinomimetics or to N-methyl-D-aspartate/glycine modulatory site agonists. Herein, we examined the effects of ***sigma1*** ***receptor*** ligands on the beta25-35 peptide-induced amnesia. The effects of neuro(active) steroids, which interact in vitro and in vivo with ***sigma1*** ***receptors*** were examined in parallel. Mnesic capacity was evaluated seven days after
administration of aggregated beta25-35 peptide (3 nmol), using spontaneous
alternation in the Y-maze for spatial short-term memory, or after 14 days,
using the step-down type passive avoidance test for long-term memory. The
sigma1 ***receptor*** agonists (+)-pentazocine, PRE-084, or
SA4503 attenuated, in a dose-dependent and bell-shaped manner, the beta25-35 peptide-induced deficits on both tests. These effects were antagonized by haloperidol or BMY-14802, confirming the ***sigma1***
receptor pharmacology. Pregnenolone, dehydroepiandrosterone, and
their sulphate esters, but not progesterone, also dose-dependently attenuated the beta25-35 peptide-induced deficits. Progesterone blocked
the beneficial effects of each other neurosteroid, behaving as an antagonist. Furthermore, haloperidol blocked the effects induced by neurosteroids, whereas progesterone antagonized the effects of the non-steroidal ***sigma1*** ***receptor*** agonists, showing a clear crossed pharmacology of different drug classes. These results demonstrate that: (i) the anti-amnesic effect of ***sigma1***
receptor agonists may be of therapeutic relevance in pathological
states affecting the cholinergic and/or glutamatergic systems, such as in pathological aging; (ii) neurosteroids play an important role in learning processes and may collectively constitute a therapeutic target; (iii) the interaction between sigma1 systems and neurosteroids appears indeed of
behavioural relevance.

L3 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:619310 CAPLUS
DOCUMENT NUMBER: 139:287042
TITLE: Cloning of an emopamil-binding protein (EBP)-like protein that lacks sterol .DELTA.8-.DELTA.7 isomerase activity
AUTHOR(S): Moebius, Fabian F.; Fitzky, Barbara U.; Wietzorrek,
Georg; Haidekker, Alexander; Eder, Andrea; Glossmann, Hartmut
CORPORATE SOURCE: Institut fuer Biochemische Pharmakologie, Innsbruck,
A-6020, Austria
SOURCE: Biochemical Journal (2003), 374(1), 229-237
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB EBP (emopamil-binding protein) is a high-affinity binding protein for [3H]emopamil and belongs to the family of so-called sigma receptors. Mutations that disrupt EBP's 3. ***beta*** .-hydroxysteroid sterol .DELTA.8-.DELTA.7 isomerase activity (EC 5.3.3.5) impair cholesterol
biosynthesis and cause X-chromosomal dominant chondrodysplasia punctata.
The authors identified a human cDNA for a novel EBPL (EBP-like protein)
with a calcd. mass of 23.2 kDa. Amino acid sequence alignments and phylogenetic anal. revealed that EBPL is distantly related to EBP (31% identity and 52% similarity) and found in animals but not in plants. EBPL
is encoded by four exons on human chromosome 13q14.2 covering 30.7 kb, and
a partially processed EBPL pseudogene was found on 16q21. The EBPL mRNA
was expressed ubiquitously and most abundant in liver, lung and kidney Upon heterologous expression in yeast EBPL had no detectable 3.
beta .-hydroxysteroid sterol .DELTA.8-.DELTA.7 isomerase and
sigma-ligand-binding activity. Nine out of ten amino acid residues essential for catalytic activity of EBP were conserved in EBPL. Replacement of the only differing residue (EBP-Y111W) reduced catalytic
activity of EBP. Transfer of the divergent residue from EBP to EBPL (EBPL-W91Y) and chimerization of EBP and EBPL at various positions failed
to restore catalytic activity of EBPL. Chem. crosslinking induced homodimerization of EBPL and EBP. Whereas mevinolin increased the mRNA
for EBP and DHCR7 (.DELTA.7-sterol reductase) in HepG2 cells, it had no
effect on mRNAs for EBPL and ***sigma1*** ***receptor*** , indicating that EBP and EBPL expression are not coordinated. The authors
propose that EBPL has a yet-to-be-discovered function other than cholesterol biosynthesis.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:375472 CAPLUS
DOCUMENT NUMBER: 139:160091
TITLE: .sigma.1 Receptor-related neuroactive steroids modulate cocaine-induced reward
AUTHOR(S): Romieu, Pascal; Martin-Fardon, Remi; Bowen, Wayne D.;
Maurice, Tangui
CORPORATE SOURCE: Centre National de la Recherche Scientifique Unite
Mixte de Recherche 5102, University of Montpellier II, Montpellier, 34095/5, Fr.
SOURCE: Journal of Neuroscience (2003), 23(9), 3572-3576
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .sigma.1 receptor is critically involved in the rewarding effect of cocaine, as measured using the conditioned place preference (CPP) procedure in mice. Neuroactive steroids exert rapid neuromodulatory

effects in the brain by interacting with GABAA, NMDA, and .sigma.1 receptors. At the .sigma.1 receptor level, 3. ***beta*** .-hydroxy-5-androsten-17-one [dehydroepiandrosterone (DHEA)] and 3. ***beta*** .-hydroxy-5-pregnen-20-one (pregnenolone) act as agonists, whereas 4-pregnene-3,20-dione (progesterone) is an efficient antagonist. The present study sought to investigate the action of neuroactive steroids in acquisition of cocaine-induced CPP in C57BL/6 mice. None of these steroids induced CPP alone. However, pretreatment with DHEA or pregnenolone (5-20 mg/kg, s.c.) during conditioning with cocaine (10 mg/kg, i.p.) increased the conditioned score. On the contrary, pretreatment with either progesterone (10 or 20 mg/kg, s.c.) or finasteride (25 mg/kg, twice a day), a 5.alpha.-reductase inhibitor, blocked acquisition of cocaine (20 mg/kg)-induced CPP. A crossed pharmacol. was obsd. between steroids and .sigma.1 ligands. The .sigma.1 antagonist N-[2-(3,4-dichlorophenyl)ethyl]-N-methyl-2-(dimethylamino)ethylamine blocked cocaine-induced CPP and its potentiation by DHEA or pregnenolone. Progesterone blocked cocaine-induced CPP and its potentiation by the .sigma.1 agonist igmesine. These results showed that neuroactive steroids play a role in cocaine-induced appetence, through their interaction with the .sigma.1 receptor. Therefore, neuroendocrine control of cocaine addiction may not involve solely glucocorticoids. The importance of neuroactive steroids as factors of individual vulnerability to drug addiction should, thus, be considered.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:216650 CAPLUS
DOCUMENT NUMBER: 138:336192
TITLE: IL-10 Mediates ***Sigma1*** ***Receptor*** -Dependent Suppression of Antitumor Immunity
AUTHOR(S): Zhu, Li X.; Sharma, Sherven; Gardner, Brian; Escuadro, Brian; Atianzar, Kimberly; Tashkin, Donald P.; Dubinett, Steven M.
CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA, 90095, USA
SOURCE: Journal of Immunology (2003), 170(7), 3585-3591
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sigma receptors are unique endoplasmic reticulum proteins that mediate signaling for a variety of drugs. The authors detd. the effect of ***sigma1*** ***receptor*** agonists on immune responses in a syngeneic lung cancer model. ***Sigma1*** ***receptor*** agonists, including cocaine, up-regulated splenocyte IL-10 mRNA and protein prodn. in vitro in a sigma receptor-dependent, pertussis toxin-sensitive manner. In vivo, ***sigma1*** ***receptor*** agonists promoted tumor growth and induced IL-10 at the tumor site. Increased tumor growth was prevented by administration of specific Abs to IL-10 or by administration of specific ***sigma1*** ***receptor*** antagonists. The authors report that ***sigma1*** ***receptor*** ligands, including cocaine, augment tumor growth through an IL-10 dependent mechanism.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:12042 CAPLUS
DOCUMENT NUMBER: 138:248840
TITLE: .sigma.1 receptor agonist-mediated regulation of N-methyl-D-aspartate-stimulated [3H]dopamine release is dependent upon protein kinase C
AUTHOR(S): Nuwayhid, Samer J.; Werling, Linda L.
CORPORATE SOURCE: Department of Pharmacology, The George Washington University Medical Center, Washington, DC, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 304(1), 364-369
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have previously shown that .sigma.1 receptor agonists inhibit N-methyl-D-aspartate (NMDA)-stimulated [3H]dopamine from slices of rat striatum in a concn.-related manner and that the inhibition is reversed by .sigma.1 receptor-selective and nonsubtype-selective .sigma. receptor antagonists. Based on previous evidence from the authors' lab. as well as other labs., the authors hypothesized that .sigma.1 receptors might use a protein kinase C (PKC) signaling pathway to modulate stimulated dopamine release. The authors tested several inhibitors of PKC isoenzymes, as well as a phospholipase C inhibitor for their effects on .sigma.1 receptor agonist-mediated regulation of [3H]dopamine release. Although none of the inhibitors tested affected the ability of NMDA to stimulate [3H]dopamine release, they all abolished regulation by the .sigma.1 receptor agonist (+)-pentazocine in a concn.-related manner. The authors also found that prior exposure to 1 .mu.M phorbol 2-myristate 13-acetate for 30 min abolished regulation by (+)-pentazocine. The authors concluded that an intact PKC system was required for .sigma.1 agonist-mediated regulation of NMDA-stimulated [3H]dopamine release from rat striatal slices. Based on the pharmacol. profile of the PKC inhibitors tested, as well as reports in the literature on PKC involvement in neurotransmitter release and .sigma. receptor action, PKC. ***beta*** . seems most likely to be responsible, at least in part, for the effects of (+)-pentazocine on dopamine release.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:634631 CAPLUS
DOCUMENT NUMBER: 138:348561
TITLE: Enhanced antidepressant effect of sigma1 (.sigma.1) receptor agonists in . ***beta*** .25-35-amyloid peptide-treated mice
AUTHOR(S): Urani, Alexandre; Romieu, Pascal; Roman, Francois J.; Maurice, Tangui
CORPORATE SOURCE: Behavioural Neuropharmacology Group, INSERM U.336, Institut de Biologie, Montpellier, 34060, Fr.
SOURCE: Behavioural Brain Research (2002), 134(1,2), 239-247
CODEN: BBREDI; ISSN: 0166-4328
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study examd. the antidepressant efficacy of the selective .sigma.1 receptor agonists igmesine or PRE-084 in mice injected intracerebroventricularly (i.c.v.) with . ***beta*** .25-35-amyloid peptide and submitted to the forced swim test. . ***beta*** .25-35 Peptide-injected animals developed memory deficits after 8 days contrarily to controls injected with scrambled . ***beta*** .25-35 peptide or vehicle soln. In the forced swim test, the i.c.v. treatment failed to affect the immobility duration, but the antidepressant effect of the .sigma.1 agonists was facilitated in . ***beta*** .25-35 animals. Igmesine reduced immobility duration at 30 vs. 60 mg/kg in control groups. PRE-084 decreased immobility duration at 30 and 60 mg/kg only in . ***beta*** .25-35 animals. Desipramine reduced the immobility duration similarly among groups and fluoxetine appeared less potent in . ***beta*** .25-35 animals. The . ***beta*** .25-35 animals exhibited decreased progesterone levels in the hippocampus (-47%). The behavioral efficacy of .sigma.1 agonists is known to depend on neuro(active)steroids levels synthesized by glial cells and neurons, which are affected by the . ***beta*** .-amyloid toxicity. This behavioral study suggests that .sigma.1 agonists, due to their enhanced efficacy, may allow to alleviate the depressive symptoms assocd. with Alzheimer's disease.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:709266 CAPLUS
DOCUMENT NUMBER: 136:382245
TITLE: [11C]Raclopride binding was reduced in vivo by ***sigma1*** ***receptor*** ligand SA4503 in the mouse brain, while [11C]SA4503 binding was not by raclopride
AUTHOR(S): Ishiwata, K.; Kobayashi, T.; Kawamura, K.; Matsuno, K.; Senda, M.
CORPORATE SOURCE: Positron Medical Center, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan
SOURCE: Nuclear Medicine and Biology (2001), 28(7), 787-792
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB [11C]Raclopride is widely used as a representative dopamine D2-like receptor ligand in positron emission tomog. (PET) studies, and [11C]1-(3,4-dimethoxyphenethyl)-4-(3-phenylpropyl)piperazine dihydrochloride ([11C]SA4503) is a recently developed selective ligand for mapping ***sigma1*** ***receptors*** in the brain. The striatal uptake of [11C]raclopride in mice was reduced by co-injection of an excess amt. of SA4503, in spite of the fact that raclopride had no effect on the brain uptake of [11C]SA4503 as shown in a previous study. The blocking effect of SA4503 on the striatal uptake of [11C]raclopride was dose-dependent, but disappeared by 1 h or 6 h after i.p. injection of SA4503. The brain uptake of [11C]SA4503 was not affected by a dopamine transporter inhibitor GBR 12909, nor was [11C]. ***beta*** .-CIT-FP inhibited by SA4503. The IC50 values of raclopride for sigma1 and sigma2 receptor subtypes measured in vitro were 11800 nM and 4950 nM, resp., suggesting that the affinity was too low for [11C]raclopride to bind in vivo to sigma receptors. On the other hand, the IC50 value of SA4503 for dopamine D2 receptors was 470 nM, that is approx. 1/25 of the affinity of raclopride for the dopamine D2 receptors. Therefore, possible explanations for the partial blocking effects of SA4503 on the striatal uptake of [11C]raclopride are: (1) an excess amt. of SA4503 may reduce the [11C]raclopride uptake due to its low affinity for dopamine D2 receptors, or (2) SA4503 may enhance endogenous dopamine release, which results in the competitive inhibition of the [11C]raclopride uptake. These finding support that both [11C]raclopride and [11C]SA4503 are selective in vivo ligands for dopamine D2-like receptors and ***sigma1*** ***receptors*** , resp., in spite of the partial blocking effect of SA4503 on the striatal uptake of [11C]raclopride.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:255286 CAPLUS
DOCUMENT NUMBER: 133:53926
TITLE: Immunocytochemical localization of the ***sigma1*** ***receptor*** in the adult rat central nervous system
AUTHOR(S): Alonso, G.; Phan, V.-L.; Guillemain, I.; Saunier, M.; Legrand, A.; Anoal, M.; Maurice, T.
CORPORATE SOURCE: INSERM Unite 336, Developpement, Plasticite et Vieillissement du Systeme Nerveux, Montpellier, Fr.
SOURCE: Neuroscience (Oxford) (2000), 97(1), 155-170
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To characterize the localization of the ***sigma1*** ***receptor*** in the adult rat central nervous system, a polyclonal antibody was raised against a 20 amino acid peptide, corresponding to the fragment 143-162 of the cloned ***sigma1*** ***receptor*** protein. Throughout the rostrocaudal regions of the central nervous system extending from the olfactory bulb to the spinal cord, intense to moderate immunostaining was found to be assocd. with: (i) ependymocytes bordering the entire ventricular system, and (ii) neuron-like structures located within the parenchyma. Double fluorescence studies confirmed that, throughout the parenchyma, ***sigma1*** ***receptor*** -immunostaining was essentially assocd. with neuronal structures immunostained for the neuronal marker . ***beta*** .III-tubulin. In all rats examd., high levels of immunostaining were always assocd. with neurons located within specific regions including the granular layer of the olfactory bulb, various hypothalamic nuclei, the septum, the central gray, motor nuclei of the hindbrain and the dorsal horn of the spinal cord. In contrast, only faint immunostaining was assocd. with neurons located in the caudate-putamen and the cerebellum. Electron microscope studies indicated that ***sigma1*** ***receptor*** immunostaining was mostly assocd. with neuronal perikarya and dendrites, where it was localized to the limiting plasma membrane, the membrane of mitochondria and of some cisternae of the endoplasmic reticulum. At the level of synaptic contacts, intense immunostaining was assocd. with postsynaptic structures including the postsynaptic thickening and some polymorphous vesicles, whereas the presynaptic axons were devoid of immunostaining. These data indicate that the ***sigma1*** ***receptor*** antibody prepd. here, represents a promising tool for further investigating the role of .sigma.1 receptors.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:507828 CAPLUS
DOCUMENT NUMBER: 131:255271
TITLE: Intracellular .sigma.1 receptor modulates phospholipase C and protein kinase C activities in the brainstem
AUTHOR(S): Morin-Surun, M. P.; Collin, T.; Denavit-Saubie, M.; Baulieu, E.-E.; Monnet, F. P.
CORPORATE SOURCE: Institut Alfred Fessard, Gif-sur Yvette, 91198, Fr.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(14), 8196-8199
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Most physiol. effects of .sigma.1 receptor ligands are sensitive to pertussis toxin, suggesting a coupling with cell membrane-bound G proteins. However, the cloning of the .sigma.1 receptor has allowed the identification of an intracellular protein anchored on the endoplasmic reticulum. Here, we show, using the isolated adult guinea pig brainstem prepn., that activation of the .sigma.1 receptor results in its translocation from the cytosol to the vicinity of the cell membrane and induces a robust and rapid decrease in hypoglossal activity, which is mediated by phospholipase C. The subsequent activation of protein kinase C. ***beta*** .1 and . ***beta*** .2 isoforms and the phosphorylation of a protein of the same mol. wt. as the cloned .sigma.1 receptor lead to a desensitization of the .sigma.1 motor response. Our results indicate that the intracellular .sigma.1 receptor regulates several components implicated in plasma membrane-bound signal transduction. This might be an example of a mechanism by which an intracellular receptor modulates metabotropic responses.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:419391 CAPLUS
DOCUMENT NUMBER: 131:96849
TITLE: Anti-amnesic effects of sigma (.sigma.)-receptor agonists
AUTHOR(S): Matsuno, Kiyoshi
CORPORATE SOURCE: Discovery Res. Div., Santen Pharm. Co., Ltd., Osaka, 533-8651, Japan
SOURCE: Nippon Yakurigaku Zasshi (1999), 114(1), 25-33
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 50 refs. Both traditional and novel sigma (.sigma.)-receptor agonists have been reported to possess anti-amnesic effects in rodents. In particular, the anti-amnesic effects induced by the novel ***sigma1*** - ***receptor*** agonists, such as (+)-pentazocine, SA4503, and PRE-084, were shown in . ***beta*** . amyloid-peptide-induced, basal forebrain (BF) lesioned and carbon monoxide (CO)-induced amnesia models and senescence-accelerated mouse (SAM). In addn., these ***sigma1*** - ***receptor*** agonists have good profiles for the central acetylcholine and dopamine systems. Moreover, they also have neuroprotective and anti-depressive effects. These evidence suggested that the ***sigma1*** - ***receptor*** agonists may be promising compds. for the treatment of dementing disorders such as Alzheimer's disease, senile dementia, and vascular dementia. However, the sigma-receptor family is still considered to be enigmatic mol. targets. More mol. cloning and biochem. studies on the sigma-receptor family are needed.

L3 ANSWER 19 OF 21 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2000131045 EMBASE
TITLE: Immunocytochemical localization of the ***sigma1*** ***receptor*** in the adult rat central nervous system.
AUTHOR: Alonso G.; Phan V.-L.; Guillemain I.; Saunier M.; Legrand A.; Anoal M.; Maurice T.
CORPORATE SOURCE: T. Maurice, Developpement, Vieillissement Systeme Nerveux, INSERM Unite 336, Montpellier, France
SOURCE: Neuroscience, (2000) 97/1 (155-170).
Refs: 41
ISSN: 0306-4522 CODEN: NRSCDN
PUBLISHER IDENT.: S 0306-4522(00)00014-2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In order to characterize the localization of the ***sigma1*** ***receptor*** in the adult rat central nervous system, a polyclonal antibody was raised against a 20 amino acid peptide, corresponding to the fragment 143-162 of the cloned ***sigma1*** ***receptor*** protein. Throughout the rostrocaudal regions of the central nervous system extending from the olfactory bulb to the spinal cord, intense to moderate immunostaining was found to be associated with: (i) ependymocytes bordering the entire ventricular system, and (ii) neuron-like structures located within the parenchyma. Double fluorescence studies confirmed that, throughout the parenchyma, ***sigma1*** ***receptor*** -immunostaining was essentially associated with neuronal structures immunostained for the neuronal marker . ***beta*** .III-tubulin. In all rats examined, high levels of immunostaining were always associated with neurons located within specific regions including the granular layer of the olfactory bulb, various hypothalamic nuclei, the septum, the central gray, motor nuclei of the hindbrain and the dorsal horn of the spinal cord. In contrast, only faint immunostaining was associated with neurons located in the caudate-putamen and the cerebellum. Electron microscope studies indicated that ***sigma1*** ***receptor*** immunostaining was mostly associated with neuronal perikarya and dendrites, where it was localized to the limiting plasma membrane, the membrane of mitochondria and of some cisternae of the endoplasmic reticulum. At the level of synaptic contacts, intense immunostaining was associated with postsynaptic structures including the postsynaptic thickening and some polymorphous vesicles, whereas the presynaptic axons were devoid of immunostaining.These data indicate that the ***sigma1*** ***receptor*** antibody prepared here, represents a promising tool for further investigating the role of .sigma.1 receptors. Copyright (C) 2000 IBRO.

L3 ANSWER 20 OF 21 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 1999247997 EMBASE
TITLE: Anti-amnesic effects of sigma (.sigma.) -receptor agonists.
AUTHOR: Matsuno K.
CORPORATE SOURCE: K. Matsuno, Discovery Research Division, Santen Pharmaceutical Co., Ltd., Shimoshinjo, Higashiyodogawa, Osaka 533-8651, Japan
SOURCE: Folia Pharmacologica Japonica, (1999) 114/1 (25-33).
Refs: 50
ISSN: 0015-5691 CODEN: NYKZAU
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB Both traditional and novel sigma (.sigma.)-receptor agonists have been reported to possess anti-amnesic effects in rodents. In particular, the anti- amnesic effects induced by the novel ***sigma1*** - ***receptor*** agonists, such as (+)- pentazocine, SA4503 and PRE-084, were shown in . ***beta*** . amyloid-peptide-induced, basal forebrain (BF)lesioned and carbon monoxide (CO)-induced amnesia models and senescence-accelerated mouse (SAM). In addition, these ***sigma1*** - ***receptor*** agonists have good profiles for the central acetylcholine and dopamine systems. Moreover, they also have neuroprotective and anti-depressive effects. These evidence suggested that the ***sigma1*** - ***receptor*** agonists may be promising compounds for the treatment of dementing disorders such as Alzheimer's disease, senile dementia and vascular dementia. However, the sigma-receptor family is still considered to be enigmatic molecular targets. More molecular cloning and biochemical studies on the sigma-receptor family are needed.

L3 ANSWER 21 OF 21 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 94382870 EMBASE
DOCUMENT NUMBER: 1994382870
TITLE: Selective antagonism of opioid analgesia by a sigma system.
AUTHOR: Chien C.-C.; Pasternak G.W.
CORPORATE SOURCE: Department of Neurology, Memorial Sloan-Kettering Cancer Ctr., 1275 York Avenue,New York, NY 10021, United States
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1994) 271/3 (1583-1590).
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB (+)Pentazocine antagonizes morphine analgesia as potently as its (-) isomer, ruling out an opioid receptor mechanism of action and suggesting, which suggests a role for ***sigma1*** ***receptors*** . Systemic (+) pentazocine also reverses supraspinal or spinal morphine analgesia. 1,3-Di(2-tolyl)guanidine, a sigma ligand with no appreciable opioid receptor affinity, antagonizes morphine analgesia. The actions of both (+)pentazocine and 1,3-di(2- tolyl)guanidine are reversed by haloperidol, which has high affinity for both sigma and D2 receptors, but not by the D2-selective antagonist (-)sulpiride, which lacks activity at sigma sites. The antiopioid sigma system is tonically active. Haloperidol, but not (-)sulpiride, decreases morphine ED50 almost 2-fold. The antiopioid system modulates only mu analgesia. Unlike analgesia, (+)pentazocine does not influence morphine's inhibition of gastrointestinal transit or lethality. (+)Pentazocine also antagonizes kappa1, kappa3 and delta analgesia through sigma mechanisms in a haloperidol-sensitive manner. (-)Sulpiride is inactive. Alone, haloperidol enhances kappa1, kappa3 and delta analgesia more dramatically than morphine, which indicates that the sigma system is active against all opioid analgesic systems. Sigma systems are responsible for some strain differences in kappa receptor sensitivity. Unlike CD-1 mice, BALB-C mice are relatively insensitive toward the kappa1 agent U50,488H and the kappa3 analgesic naloxone benzoylhydrazone. Blockade of the sigma system with haloperidol eliminates these strain differences. In conclusion, sigma1 systems functionally antagonize opioid analgesia without affecting morphine's effects on gastrointestinal transit or lethality. The antiopioid sigma system is tonically active and is more active against kappa analgesia than mu. The level of this tonic activity plays a significant role in strain differences in analgesic sensitivity toward opioid analgesia.